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Documents Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane, Room 1061
Rockville, Maryland 20852

RE: COMMENT ON DRAFT GUIDANCE – Drugs, Biologics, and Medical Devices Derived from Bioengineered Plants for Use in Humans and Animals
Docket # 02-D-0324

The following comments and suggestions are submitted by the Iowa Cooperative, a 73 member farmer cooperative association organized pursuant to Chapter 499 of the Code of Iowa.

Federal agency questions or response to these comments may be addressed to Gary Henderson, Project Coordinator, Box 692, 1422 Central Avenue, Fort Dodge, Iowa 50501, telephone 515-228-3432, or e-mail: ghlb@huxcomm.net.

Members of the Iowa Cooperative have carried out field production of plant made pharmaceuticals (PMP) in corn under APHIS Movement Permit #01-057-01m, and Release Permit #01-057-01r. Our comments and suggestions are made with respect to the experience gained in the successful pursuit of those permitted activities.

1. Contamination of Food/Feed Crops By Non-food Material

Page 3 of the Draft Guidance, under General Considerations (lines 223-226), acknowledges that current provisions of the Food, Drug and Cosmetic Act (21 USC 342) are now interpreted to the effect that presence of non-food, non-feed material in food or feed could render such products adulterated. As noted in recent enforcement actions, such adulterated products are therefore subject to condemnation, and civil and criminal penalties can be levied against persons responsible.

Inclusion of this statement in the Draft Guidance implies continued adherence to a policy of zero tolerance for commingling of regulated material in food/feed products. We do not question the legal authority of the statement or its implication. However, we suggest that an additional provision should be included to reflect a willingness of FDA to entertain submission of data to support establishment of appropriate tolerances for inclusion of certain specific PMP material in food/feed products.

We recognize that this is a potentially troublesome issue since it is an implicit acknowledgement that unintended mixing of PMP material may occur in food/feed products. The use of data to characterize the hazard level of specific PMP materials should operate on the same principles now applied to other residual materials in food or feed. Under those established, science-based principles, a zero tolerance policy for all PMP materials should no longer be necessary.

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For our part, the Iowa Cooperative seeks to join with others to support rigorous scientific research and risk-benefit analysis for a range of PMP materials and the potential exposure levels that may occur in food/feed products. This effort, it is hoped, would serve as a basis for later development of appropriate regulatory tolerances for specific residual PMP materials within grain crops intended for food/feed use.

2. Regional Production Restriction

The Draft Guidance, page 9, lines 489-90, proposed consideration of growing plant made pharmaceutical (PMP) crops that outcross in regions of the country where little or none of food/feed counterparts are grown. Our experience strongly indicates that such a restriction would be of little or no value in assuring containment of PMP material. It is highly likely that any region with inherent suitability for corn production has been and will be so used, so that other non-PMP corn crops will exist in some proximity. It is also important to note that many remote growing regions not utilized for food/feed production, are commonly used for production of seed corn, where the negative impact of pollen contamination is potentially more damaging than in locations devoid of seed production.

The far more effective approach to pollen or grain product containment will be found in establishment of production and handling requirements within APHIS permits. Those requirements can include multiple redundant measures to assure containment, including spatial separation of PMP crops, border rows, temporal planting separation, detasseling, use of male sterile lines, insistence on use of dedicated planting, harvesting, and transport equipment, etc.

Our experience supports the view that adherence to such multiple redundant containment measures provides the most positive assurance of pollen containment. We suggest that the Draft Guidance be modified to report intent to invoke such multiple redundant containment requirements as the preferred approach to this issue, and to delete the sentence now found in lines 489-90.

3. Consideration of Fencing for Field-Grown Plants

The Draft Guidance, on page 10, lines 533-534, proposes consideration of perimeter fencing as a means of excluding wildlife and escaped livestock from entering fields producing PMP crops. Security fencing is unlikely to provide the enhanced security that the Draft Guidance is seeking. A requirement for use of a type of security fencing not commonly found in an agricultural area would serve as a public notice of the use of property for PMP production, making that fenced property a more likely target for vandalism. Furthermore, the most common species of foraging wildlife may easily climb security fencing (raccoon, squirrel, opossum), or as in the most likely case of birds, would be altogether unaffected by fencing of any kind. By utilizing the USDA developed Technology Protection System(terminator gene), any dispersal of the seed would not result in volunteer plants. Additional research in this area is necessary to further safeguard the entire process.

We suggest that this measure be revised in favor of an alternative that would emphasize production of PMP crops in locations removed by some specified distance from fields where livestock are commonly released to pasture and from forested areas of wildlife habitat.

4. Confinement Measures

Within Section C, subsections 3 and 4 address Field Grown Plants and Control of Harvested Material, respectively. The PMP production experience of our members leads us to support the provisions of those subsections. Lines 524-525, specifically, call attention to the need for adequate training of all persons involved in field growth. Based on our knowledge of recent enforcement actions in Iowa and Nebraska, we think it reasonable to conclude that failure of adequate training of all persons involved was the principal contributing factor in the permit violations that precipitated those incidents.

The Iowa Cooperative has undertaken extensive effort to develop training methods and materials specific to PMP production. Our initiative is also cooperating with the Novecta program for grower training sponsored by the Iowa and Illinois' Corn Growers Associations. Based on those experiences, we suggest a possible modification of provisions on lines 524-525 to provide that persons to be involved in field growth should be carefully selected according to knowledge of plant physiology and thoroughly trained to perform the duties for which they are responsible.

5. Product Manufacturing Procedures – Growth Conditions, Harvest, Transfer and Storage

Section D of the Draft Guidance, specifically subsections 2, 3 and 4, contain recommendations for documentation of conditions and variables that bear upon the PMP production process. We wish to report that the experience gained by members of the Iowa Cooperative under APHIS permits cited previously confirms that the documentation recommendations of the Draft Guidance are workable and appropriate. We support establishment of those recommendations as basic policy within the regulatory process, and offer whatever assistance our organization may provide for further elaboration of regulatory policy regarding Growth Conditions, Harvest, and Transfer and Storage of PMP materials. Lines 547-548 call for the reconciliation of quantities of material leaving the growing facility and arriving at the processing facility. We utilize a Mass Balance Process at all stages starting with the harvest in the field to perform this reconciliation. We look forward to opportunities through which our field experience may serve as a demonstration platform for the federal agencies.

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